0062

Table 3. Kidney Biopsy Findings of Patients with Monoclonal Gammopathy.

Patient No.	Pattern of Injury	%Globally Sclerosed Glomerull	%Crescent	%Interstitial Fibrosis	IF Microscopy	EM
1	MPGN	5.4%	2.7%	20.0%	C3 2 + (CW)	Endotheliocyte injuried , subendothelial expansion with fluffy material
2	MPGN	55.0%	0.0%	25.0%	C3 2 + (CW and MES)	electron-dense deposits in MES and SU
3	MPGN	17.6%	0.0%	20.0%	C3 2 + (CW and MES)	electron-dense deposits in MES
4	MPGN	0.0%	0.0%	25.0%	C3 2 + (CW and MES)	subendothelial expansion with fluffy material
5	MPGN	14.9%	3.7%	10.0%	C3 2 + (CW)	electron-dense deposits in MES and SU
6	MPGN	9.1%	0.0%	5.0%	C3 2 + (CW and MES)	electron-dense deposits in MES, SU and SE
7	MPGN	28.6%	0.0%	4.0%%	C3 3 + (CW and MES)/IgG, IgM (trace)	electron-dense deposits in MES, SU

MPGN = membranoproliferative glomerulonephritis; CW = capillary wall; MES = mesangial; SE = subepithelial; SU = subendothelial.

Conclusion: Monoclonal gammopathy was a predominant cause of C3 GN in the older patients. Pattern of pathological injury was membranoproliferative. Immunodepressive therapy may be effective, but the key point of therapy should be targeting monoclonal gammopathy.

http://dx.doi.org/10.1016/j.hkjn.2015.09.010

0066

PLA2R Autoantibodies and Glomerular PLA2R Deposit in Membranous Nephropathy: How to Evaluate the Roles they Played?

H. Z. Qin, W. B. Le, M. C. Zhang, C. H. Zeng, H. Chen, Q. Ren, D. C. Chen, K. Zuo, F. Xu, Z. H. Liu
National Clinical Research Center of Kidney Diseases, Jinling Hospital, Nanjing University School of Medicine, Nanjing, Jiangsu, China

Background: Higher glomerular PLA2R-antigen deposit (GAg) rates compared with serum phospholipase A2 receptor-antibody (SAb) positive rates were reported. However, the exact roles played by these two biomarkers remain unknown.
Methods: A total of 572 patients diagnosed with IMN were included. Both SAb and GAg were detected. Fifty-two IMN patients received repeat renal biopsy were included.
Results: 572 patients, 401 (70.1%) were SAb positive (SAb+) while 171 (29.9%) were SAb negative (SAb-). In SAb+ patients, the glomerular PLA2R-antigen deposition (GAg+) was observed in 99.1% (397/401). Interestingly, the GAg+ was observed in 68.4% (117/171) Sab patients. Patients with SAb manifested more severe proteinuria (3.9 g/24 hours vs. 2.8 g/24 hours, $P < 0.001$) and lower eGFR (104 ml/min/1.73 m^2 vs. 110 ml/min/1.73 m^2, $P = 0.002$) than patients without SAb. Further comparison between SAb+/GAg+ and SAb-/GAg+ showed a similar profile. Patients with SAb+/GAg+ also showed lower chance of proteinuria remission and higher chance of renal function decline in the follow up when compared to patients with SAb-/GAg+. Changes of SAb and GAg were observed in patients with repeat renal biopsy, in 11 patients the SAb+ turned into SAb-, among them 1 patient failed to achieve remission, 7 patients achieved remission and 4 remitted during the interval but relapsed at the time of repeat biopsy. While the GAg+ turned into GAg- in only 3 patients, all achieved remission at the repeat biopsy. The proportion of GAg disappearance was lower than SAb ($P = 0.016$).
Conclusion: The GAg deposit can be detected in a large proportion of SAb negative patients, which can be explained by the lag of GAg disappearance in the follow up. SAb was more tightly correlated to disease activity, treatment response and prognosis than GAg. We recommend adopting GAg deposit detection as a supplement to SAb in IMN diagnosis and continuing to monitor SAb during follow-up.

http://dx.doi.org/10.1016/j.hkjn.2015.09.011

0074

sFlt-1 is Regulated via Both Transcriptional and Post-transcriptional Modification in Preeclampsia

W. Wang[1], N. Parchim[2], R. Luo[1], L. Tao[1], Y. Xia[2]
[1]*Department of Nephrology, Xiangya Hospital, Central South University, Changsha, Hunan Province, China*
[2]*Biochemistry and Molecular Biology Department, University of Texas Medical School at Houston, Houston, Texas, USA*

Background: Preeclampsia (PE) is a life-threatening hypertensive disorder of pregnancy. Soluble fms-like tyrosine kinase 1 (sFlt-1) is elevated and known to contribute to PE. However, molecular basis underlying its up-regulation in PE remain unclear.
Methods and Results: By using immunohistochemistry and western blot, we demonstrated hypoxia inducible factor-1α (HIF-1α), an important transcriptional factor, and U2 small nuclear ribonucleoprotein auxiliary factor 65-kilodalton subunit (U2AF65), a key factor involved in alternative splicing, are significantly increased in the placental tissue from PE patients. Using two animal models of PE including angiotensin II type 1 receptor agonistic autoantibody (AT1-AA) and LIGHT (a TNF-α superfamily member)-induced PE mouse model coupled with in vivo nanoliposome-delivery system to specifically knockdown HIF-1α and U2AF65, we found that knockdown of HIF-1α or U2AF65 siRNA significantly attenuated AT1-AA-induced hypertension (HIF-1α siRNA: 137 ± 4 mmHg; U2AF65 siRNA: 140 ± 5 mmHg vs. AT1-AA group 164 ± 3 mmHg, $p < 0.05$), proteinuria (HIF-1α siRNA: 41.6 ± 3.2 μg/mg, U2AF65 siRNA: 34.9 ± 5.3 μg/mg vs. AT1-AA group 85.9 ± 4.8 μg albumin/mg creatinine, $p < 0.05$) and circulating sFlt-1 level. Similarly, we found that HIF-1α and U2AF65 knockdown significantly reduced sFlt-1 levels, hypertension and proteinuria in LIGHT-infused pregnant mice. Finally, using splice-specific PCR assay, we found that knockdown HIF-1α significantly reduced total Flt-1 mRNA level in the placentas of both AT1-AA and LIGHT-infused pregnant mice but no effect on the ratio of sFlt-1/ Flt-1. In contrast, U2AF65 knock down significantly reduced the ratio of sFlt-1/ Flt-1 without an effect on total Flt-1 mRNA level in these two PE mouse models.
Conclusion: Overall, we have revealed two molecular basis underlying sFlt-1 inductions in PE: (1) elevated HIF-1α directly increases sFlt-1 levels under transcriptional levels; (2) elevated U2AF65 enhances alternative splicing to increase sFlt-1 levels.

http://dx.doi.org/10.1016/j.hkjn.2015.09.012

0078

Long Non-coding RNA_5318 is a Novel Therapeutic Target for Renal Fibrosis in Obstructive Nephropathy

M. Feng[1,2], P. Tang[1], Y. K. You[1], L. L. Lv[1], X. R. Huang[1], A. P. Xu[2], H. Y. Lan[1]
[1]*Department of Medicine and Therapeutics, Li Ka Shing Institute of Health Sciences, CUHK-Shenzhen Research Institute, The Chinese University of Hong Kong, Hong Kong, China*
[2]*Department of Nephrology, Sun Yat-sen Memorial Hospital, Sun Yat-Sen University, Guangzhou, China*

Objective: Long non-coding RNAs (lncRNAs) exert pathophysiologic functions in many diseases. By using RNA sequencing, we recently found that lncRNA_5318 is